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Applications of Low Dose Electron Ptychography.

AI Kirkland[1,2,3*], J. S. Kim[1,2], C. S. Allen[1,3], C. Huang[2], E Liberti[2], CM O'Leary[5], P. D. Nellist[1] and P. Wang[4]

[1.]Department of Materials, University of Oxford, Oxford, UK
[2.]Rosalind Franklin Institute, Harwell Science and Innovation Campus, Didcot, UK
[3.]Electron Physical Sciences Imaging Centre, Diamond Light Source Ltd., Harwell Science and Innovation Campus, Didcot, UK
[4.]Department of Physics, University of Warwick, Coventry CV4 7AL, UK
[5.] Department of Physics, University of California, Loss Angeles, Los Angeles, CA, United States
* Corresponding author: angus.kirkland@materials.ox.ac.uk

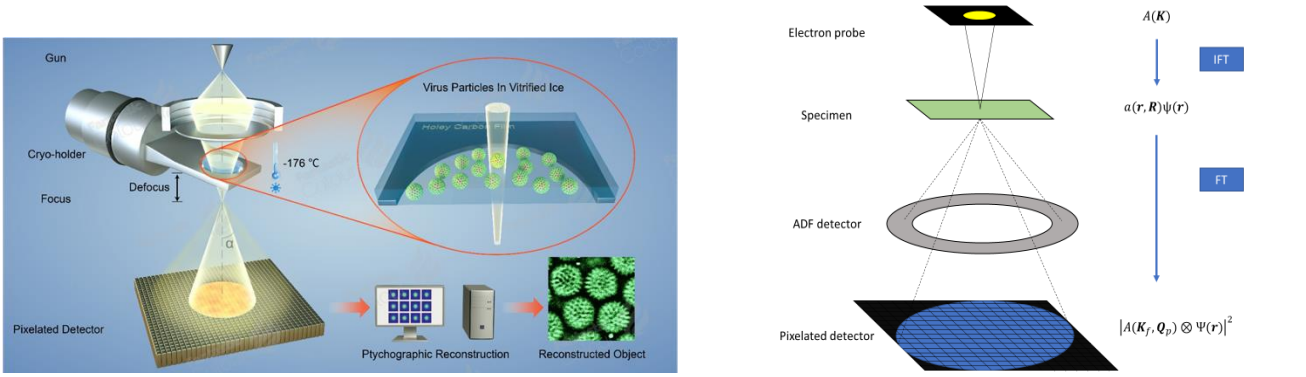
Recent development in pixelated direct electron detectors operating at high frame rates [1,2] has led to a significant increase in the use of a diverse range of 4D STEM based techniques. In all such experiments a suitably conditioned probe is scanned across a sample and an array of far field diffraction patterns are recorded. These are then generally processed to select only specific information for example, high angle scattering to synthesise an annular dark field image or the bright field disk for ptychographic reconstruction (Fig. 1).

For Ptychography various, previously described reconstruction direct methods can be used to retrieve the complex specimen transmission function including single sideband (SSB) and Wigner distribution deconvolutions (WDD) [3]. Alternatively, one of several indirect (iterative) methods including the extended Ptychographic Iterative Engine ePIE [4], which solves for both probe and object have been extensively used in electron Ptychography. Importantly, it has been shown that regardless of the reconstruction algorithm used ptychographic methods are more robust and sensitive than other phase sensitive imaging methods, likely due to the more efficient use of the information available within the dataset.

In this talk I will describe applications of electron Ptychography under low dose conditions and challenges arising in this dose regime. I will consider how the use of binary counting on a pixelated detector can be used to increase acquisition speed, taking advantage of sparsity in the recorded diffraction patterns under low dose conditions [5].

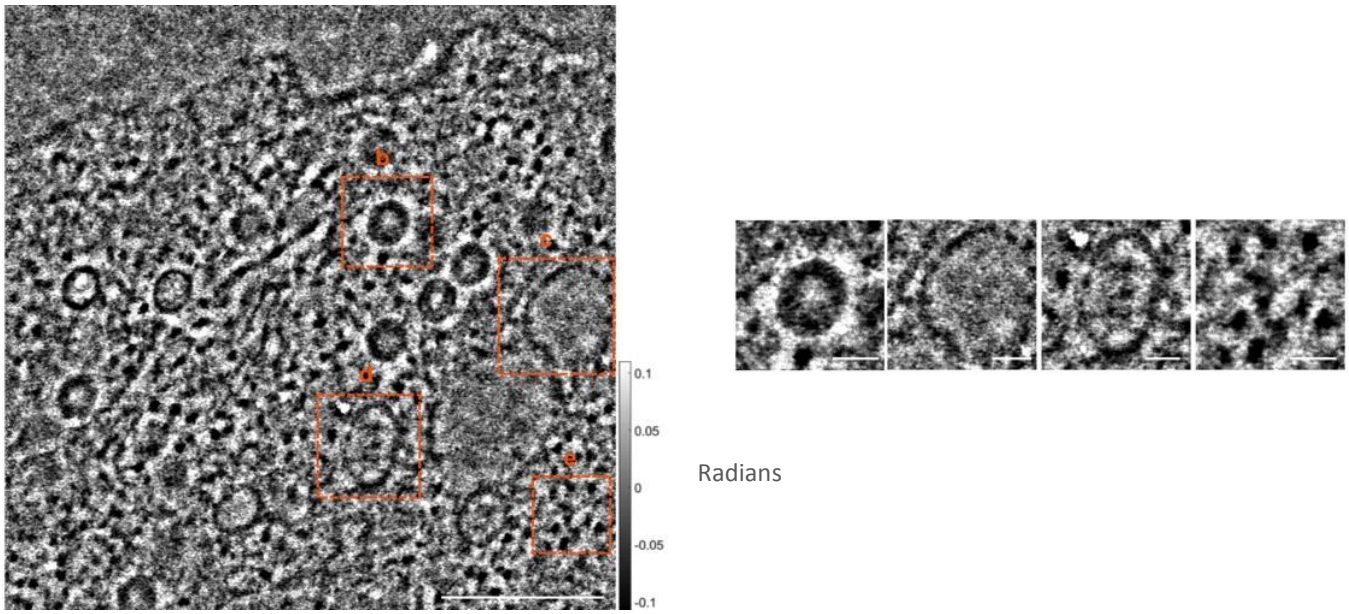
The use of Ptychography for biological systems will then be discussed with an emphasis on exploiting the phase sensitivity for 3D reconstruction of both low and high spatial frequencies in a single particle analysis approach and for recovering the object phase over wide fields of view (Fig. 2) [6]. Both of these present challenges, but are crucial to the application of this method in biology, particularly at the cellular scale.

Finally, potential future directions and improvement in the use of electron Ptychography under low dose conditions will be summarised. These include the use of AI and ML for determining noisy probe characteristics, sparse scanning geometries for additional dose reduction, combinations of data recorded with variable convergence angles for wide bandwidth reconstruction and recent applications to hybrid organic/ inorganic systems.



(a) (b)

Figure 1. (a) Schematic optical configuration diagram of the workflow used for cryo-ptychography in this case using a defocused probe. (b) The relationship between the probe and object functions to the recorded intensity.



(a) (b)

Figure 2. (a) Low-dose large scale ptychographic phase of an Adenovirus-infected cell (b) Magnified views of a viral particle, a vacant vesicle a transport vesicle and free ribosomes taken from regions indicated with orange squares in (a). Scale bars are (a) 300 nm, and (b) 50 nm.

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